

Provisional Consent to the Distribution of a New Medicine

Pursuant to section 23(1) of the Medicines Act 1981, the Minister of Health hereby provisionally consents to the sale, supply or use in New Zealand of the new medicine which was referred to the Minister of Health under the provisions of section 24(5) of the Act and set out in the Schedule hereto:

Schedule

Product:	Comirnaty (COVID-19 mRNA vaccine)
<i>Active Ingredient:</i>	BNT162b2 [mRNA] 0.5mg/mL
<i>Dosage Form:</i>	Concentrate for injection
<i>New Zealand Sponsor:</i>	Pfizer New Zealand Limited
<i>Manufacturer:</i>	Pfizer Manufacturing Belgium NV, Puurs, Belgium

Provisional consent is granted until 3 November 2021.

This consent is given subject to the following conditions:

The New Zealand Sponsor must fulfil the following obligations within the timelines specified, the dates of which may be altered by mutual agreement with Medsafe (the reference numbers have been retained from the original provisional consent conditions as per [New Zealand Gazette, 3 February 2021, Notice No. 2021-go338](#)):

- 2) The New Zealand site of batch release will only release batches for distribution in New Zealand once the sponsor has verified that the shipping temperature profile meets specifications.
- 4) Provide independent batch certification, such as UK National Institute for Biological Standards and Control (NIBSC) certification, EU Official Control Authority Batch Release (OCABR) certification, Australian TGA batch release assessment, or any other certification agreed with Medsafe, on request for all batches distributed in New Zealand.
- 5) Provide data to further characterise the truncated and modified mRNA species present in the finished product. Data are expected to cover batches used in clinical trials (for which the characterisation data could be available earlier) and the PPQ batches. These data should address results from ion pairing RP-HPLC addressing 5'cap levels and presence of the poly(A) tail. These data should also address the potential for translation into truncated S1S2 proteins/peptides or other proteins/peptides. Relevant protein/peptide characterisation data for predominant species should be provided. Any homology between translated proteins (other than the intended spike protein) and human proteins that may, due to molecular mimicry, potentially cause an autoimmune process should be evaluated. Due date: 9 August 2021.
- 6) Provide the analysis of the main peak of the RNA integrity test representing the full-length RNA, that addresses 5'cap levels and presence of the poly(A) tail. Due date: 9 August 2021.
- 7) Provide the reassessment of the active substance specification for the DNA template purity and impurities. Due date: 9 August 2021.
- 9) Comprehensively describe the capability of the next generation sequencing technology platform to detect lower amounts of RNA species of alternative sequence in the presence of the correct, more abundant RNA for the active substance. Due date: 9 August 2021.
- 10) Provide a discussion of the results and the assay suitability for the cell-based flow cytometry and the western blot method used for biological characterisation of protein expression for the active substance. Due date: 9 August 2021.
- 11) Provide additional data for the active substance to confirm the identities of the observed western blot (WB) bands obtained by the in vitro expression assay. Protein heterogeneity, resulting in broad bands on the WB and uncertainties in the theoretical intact molecular weight of the spike protein, is assumed to be due to glycosylation. Therefore, to further confirm protein identities, enzymatic deglycosylation of the expressed proteins followed by WB analysis should be performed. Correlation with the calculated molecular weights of the intact S1S2 protein should be demonstrated. Due date: 9 August 2021.
- 12) Provide a summary of the validation/verification status of the immunoblot analytical procedure used to detect double-stranded RNA (dsRNA) in the active substance. Due date: 9 August 2021.
- 13) Reassess and revise the active substance and finished product specifications acceptance limits as further data becomes available from ongoing clinical trials and in-line with manufacturing process capability and stability data of the product. Comprehensive data should be provided comprising batch analyses of a suitable number of commercial batches as well as analyses of batches that have been used in the (ongoing) clinical trials. Due date: 9 August 2021.
- 14) Introduce an active substance specification to control poly(A) tail length, which is considered a critical attribute and should be controlled on each batch. A suitable method should be developed, and appropriate acceptance criteria should be set. Due date: 9 August 2021.
- 15) Provide additional data to support the suitability of the method used for %poly(A) tail or develop and introduce an alternative suitable assay. The %poly(A) tail should be characterised following any future active substance process changes. Due date: 9 August 2021.
- 16) Revise the mRNA integrity and polydispersity finished product specifications as further data becomes available from ongoing clinical trials and in-line with manufacturing process capability. Due date: 9 August 2021.

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17) Provide additional data to support the suitability of the method used for potency determination or an alternative suitable assay for this purpose should be developed and introduced. Then the finished product acceptance criteria for potency should be revised accordingly. Due date: 9 August 2021.

18) Lipid-related impurities should be further evaluated, and an appropriate control strategy should be introduced, suitably justified and provided for assessment. Due date: 9 August 2021.

20) Provide test results of future process validation-batches of finished product tested according to the extended comparability testing protocol.

21) Expand the description of the finished product manufacturing process with the following details:

(1) when the batch size is twice the original one, the range number of active substance bags and active substance batches to be thawed, and the number of mixers should be stated,

(2) the configuration of filters used in finished product manufacture,

(3) the surface area of the sterile filter should be adapted to the batch size, unless otherwise justified,

(4) that process control for RNA content prior to dilution is important, particularly if several runs of TFF are performed in parallel with batch sizes.

Due date: 9 August 2021.

25) Provide updated finished product stability data as it becomes available, including stability data for the process performance qualification batches.

26) Provide a detailed summary of the ALC-0315 manufacturing process completed at the Avanti and Croda manufacturing sites. The differences in manufacture between the two sites will also be clearly detailed. Due date: 9 August 2021.

27) Provide a detailed description of the ALC-0315 starting materials (including the general synthetic route), the reagents and solvents used, reaction conditions, and in-process controls. If applicable, reprocessing, reworking, and recovery/reuse operations should also be detailed. Due date: 9 August 2021.

28) Provide a discussion regarding the control of the raw materials for ALC-0315. This should include the manufacture, qualified suppliers, and quality controls of the starting materials. The in-house controls applied to the raw materials and solvents used should also be detailed, as should the control of any potentially genotoxic contaminants. Due date: 9 August 2021.

29) Provide information and justification on critical steps and intermediates (including specifications) for ALC-0315. Due date: 9 August 2021.

32) Further evaluate specified impurities for ALC-0315 and include appropriate specification limits for individual impurities when more data are available. Acceptance criteria for specified and unspecified impurities should be added to the specification for ALC-0315 and should also be evaluated during stability studies. Due date: 9 August 2021.

33) Update the control of the solvent residues to those that are used in the manufacture of the ALC-0315 excipient. The solvents which are not used should be removed from the specifications. Associated changes to the analytical method should be detailed and validated where necessary. Due date: 9 August 2021.

34) Update the ALC-0315 assay and impurities limits when additional supporting data is available. Due date: 9 August 2021.

35) Provide detailed method validation reports for assay, impurities, and residual solvents for ALC-0315. Due date: 9 August 2021.

36) Provide ALC-0315 impurity standard information for any identified impurities reported. Due date: 9 August 2021.

37) Provide a retest period and storage condition for ALC-0315 based on stability data. Due date: 9 August 2021.

38) Provide updated stability data for ALC-0315 manufactured at the Avanti and Croda sites. Due date: 9 August 2021.

40) Provide information regarding the control of ALC-0159 raw materials. This should include the manufacture, qualified suppliers, and quality controls of the starting materials. The in-house controls applied to the raw materials used should also be detailed, as should the control of any potentially genotoxic contaminants. Due date: 9 August 2021.

41) Provide information and justification on critical steps and intermediates (including specifications) for ALC-0159. Due date: 9 August 2021.

42) Provide a discussion regarding process development for ALC-0159 with particular emphasis on identification and purge of impurities. Due date: 9 August 2021.

45) Update the control of the solvent residues to those that are used in the manufacture of the ALC-0159 excipient. The solvents which are not used should be removed from the specifications. Associated changes to the analytical method should be detailed and validated where necessary. Due date: 9 August 2021.

46) Update the ALC-0159 assay and impurities limits when additional supporting data is available. Due date: 9 August 2021.

47) Further evaluate specified impurities for ALC-0159 and include appropriate specification limits for individual

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impurities when more data are available. Acceptance criteria for specified and unspecified impurities should be added to the specification for ALC-0159 and should also be evaluated during stability studies. Due date: 9 August 2021.

48) Provide detailed method validation reports for assay, impurities and residual solvents for ALC-0159. Due date: 9 August 2021.

49) Provide impurity standard information for any identified impurities reported for ALC-0159. Due date: 9 August 2021.

51) Provide updated stability data for ALC-0159. Due date: 9 August 2021.

52) Provide any reports on the duration of efficacy and the requirement for booster doses within five working days of these being produced.

54) Provide any reports on efficacy including asymptomatic infection in the vaccinated group, vaccine failure, immunogenicity, efficacy in population subgroups and results from post-marketing studies, within five working days of these being produced.

55) Provide the final Clinical Study Reports for Study C4591001 and Study BNT162-01 within five working days of these being produced.

56) Provide Periodic Safety Update Reports according to the same schedule as required by the EMA.

57) Provide monthly safety reports, as well as all safety reviews they conduct or become aware of.

58) Perform the required pharmacovigilance activities and interventions detailed in the agreed RMP and any agreed updates to the RMP. An RMP should be submitted at the request of Medsafe or whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important milestone being reached.

Dated this 21st day of June 2021.

CHRIS JAMES, Group Manager, Medsafe, Ministry of Health (pursuant to delegation given by the Minister of Health on 11 September 2013).